

**REMARKS**

Upon entry of the amendment, claims 1-11, 13, 17-23, and 42-45 will be pending. Claims 1, 3, 9, and 13 are amended herein, and claim 45 is newly added. A marked-up copy showing the amendment to the specification and the claims is attached hereto as Exhibit A.

The amendments submitted herewith are supported by the specification and original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendments is respectfully requested.

**Claim Rejection under 35 U.S.C. § 112, First Paragraph**

Claims 1-11, 13, 14, and 17-23 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

In response to the Applicants amendments and arguments in the Response filed February 12, 2002, the Office Action asserts that the rejected claims do not meet the written description requirement because it is allegedly not clear that all sequences that hybridize with SEQ ID NO:1 under stringent conditions have a regulatory activity in endothelial cells. Furthermore, it is alleged that the specification does not provide an adequate written description of the rejected claims because Applicant has not provided an example of a DNA

molecule that hybridizes under stringent conditions to SEQ ID NO:1, and functions to regulate expression *in vivo* in endothelial cells.

Claims 1-11, 13, 14, and 17-23, no longer recite nucleotide sequences which hybridize to the recited sequences of SEQ ID NO:1. Therefore, with respect to these claims, the Office Action's allegations related to a lack of written description are moot.

With respect to claim 3, the Office Action alleges that this claim encompasses all sequences that hybridize to SEQ ID NO:1 under stringent conditions. However, claim 3 does not recite sequences that hybridize to SEQ ID NO:1. Therefore, Applicants respectfully disagree with the Office Action's assertion that claim 3 encompasses all sequences that hybridize to the recited fragments of SEQ ID NO:1. Therefore, the rejection to claims 1-11, 13, 14, and 17-23 under 35 U.S.C. § 112, first paragraph, has been overcome. Applicants respectfully request withdrawal of the rejection.

With respect to claims 42-44, the Office Action does not include these claims in the written description rejection. Clarification is sought as to whether these claims are included in the 35 U.S.C. § 112, first paragraph rejection.

Newly added claim 45 recites a recombinant DNA molecule that includes at least one first regulatory sequence which confers expression in endothelial cells *in vivo*, wherein the first regulatory sequence is a DNA sequence that hybridizes with a nucleotide sequence of element (i) or (ii) of claim 1 under stringent conditions. Claim 45 which includes both a structural and a functional requirement for the first regulatory sequence is adequately described by the disclosure as filed. Claim 45 recites the functional requirement that the first regulatory sequence confers expression in endothelial cells *in vivo*. Furthermore, claim 45 includes the structural requirement that the first regulatory sequence includes a nucleotide sequence that hybridizes with a nucleotide sequence of claim 1, element (i) or (ii) under stringent conditions.

Regarding the Office Action's assertion that some sequences that some DNA sequences that hybridize with a nucleotide sequence of claim 1, element (i) or (ii) under stringent conditions will not confer expression on endothelial cells, *in vivo*, DNA sequences that do not confer expression on endothelial cells *in vivo* are not encompassed by this claim. Furthermore,

In re Application of:

Breier et al.

Application No.: 09/445,201

Filed: April 12, 2000

Page 7

PATENT

Attorney Docket No.: VOSS1110

it is not required that a disclosure is of such specificity that it provides individual support for each species that the genus embraces (See e.g., MPEP § 2163).

**Claim Rejection under 35 U.S.C. § 112, Second Paragraph**

Claims 1 and 3 stand rejected under 35 U.S.C. § 112, Second Paragraph based on typographical errors in the claims. Applicants respectfully traverse this rejection. Claim 1 is amended herein to include a step (ii) and only a single step (i). Claim 3 is amended herein such that clause c does not refer to itself. Furthermore, the term "capable" has been deleted from the claim. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1 and 3 under 35 U.S.C. § 112, Second Paragraph.

In re Application of:  
Breier et al.  
Application No.: 09/445,201  
Filed: April 12, 2000  
Page 8

PATENT  
Attorney Docket No.: VOSS1110

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account  
No. 50-1355.

Respectfully submitted,

Date: September 23, 2002



Lisa A. Haile, J.D., Ph.D.

Reg. No. 38,347

Telephone: (858) 677-1456

Facsimile: (858) 677-1465

**CUSTOMER NUMBER 28213**  
**GRAY CARY WARE & FREIDENRICH LLP**  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133

Enclosures: Exhibit A

**EXHIBIT A**

**MARKED-UP COPY OF THE CLAIMS SHOWING THE AMENDMENTS**

1. (Twice Amended) A recombinant DNA molecule comprising:
  - (a) at least one first regulatory sequence which confers expression in endothelial cells in vivo, wherein said first regulatory sequence is selected from the group consisting of
    - (i) a DNA [sequences] sequence comprising a nucleotide sequence as given in SEQ ID NO: 1;
    - [(i)] (ii) a DNA [sequences] sequence comprising a nucleotide sequence of SEQ ID NO: 1 from nucleotide 8260 to nucleotide 10560, from nucleotide 8336 to nucleotide 10608 and/or from nucleotide 10094 to nucleotide 10608;  
and
    - (iii) [DNA sequences comprising a nucleotide sequence which hybridizes with a nucleotide sequence of (i) or (ii) under stringent conditions;  
and]
    - (iv)] a DNA [sequences] sequence comprising a fragment of a nucleotide sequence of (i) or (ii) [, or (iii)]; and
  - (b) operatively linked thereto a heterologous DNA sequence.

3. (Twice Amended) The recombinant DNA molecule of claim 1 or 2, wherein said first regulatory sequence is selected from the group consisting of

(a) a DNA [sequences] sequence comprising a nucleotide sequence as given in SEQ ID NO: 1;

(b) a DNA [sequences] sequence comprising a nucleotide sequence of SEQ ID NO: 1 from nucleotide 8260 to nucleotide 10560, from nucleotide 8336 to nucleotide 10608 and/or from nucleotide 10094 to nucleotide 10608; and

(c) a DNA [sequences] sequence comprising a fragment of a nucleotide sequence of any one of (a) [to (c) capable of conferring] or (b) that confers expression in endothelial cells.

9. (Twice amended) The recombinant DNA molecule of claim 5, wherein said promoter comprises a DNA sequence selected from the group consisting of

(a) a DNA [sequences] sequence comprising the nucleotide sequence as given in SEQ ID NO: 1 from nucleotide 6036 to nucleotide 6959;

(b) a DNA [sequences] sequence comprising the nucleotide sequence of the human Flk-1/KDR promoter; and

(c) [DNA sequences comprising a nucleotide sequence which hybridizes with a nucleotide sequence of (a) or (b) under stringent conditions; and

(d)] a DNA [sequences] sequence comprising a fragment of a nucleotide sequence of any one of (a) [to (c)] or (b).

13. (Twice Amended) The recombinant DNA molecule of claim 41, wherein said protein is selected from the group consisting of Vascular Endothelial Growth Factor (VEGF), Hypoxia Inducible Factors [7] (HIF), HIF-Related Factor (HRF), tissue plasminogen activator, p21 cell cycle inhibitor, nitric oxide synthase, interferon- $\gamma$ , atrial natriuretic polypeptide, [and] monocyte chemotactic proteins, luciferase, green fluorescent protein and lacZ.